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Research Article

Trends in Antibiotic Resistance in Infected Wounds: A Retrospective Analysis at the National Research Center for Traumatology and Orthopedics Named After Academician N.D. Batpenov (2021-2023)

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Abstract

The increasing incidences of antibiotic-resistant infections is a significant concern in managing complicated wound healing. This study examines the trends and microbiological profiles of infected wounds treated surgically at the National Research Center for Traumatology and Orthopedics named after Academician N.D. Batpenov in Astana, Kazakhstan, from 2021 to 2023. A retrospective analysis was conducted on patients who underwent surgical wound closure between 2021 and 2023. Data on patient age, length of hospital stay, comorbidities, type of trauma, chronicity of the condition, affected body part, initial diagnosis, and microbiological culture results were collected. The study assessed the frequency and patterns of antibiotic resistance among isolated pathogens. In 2021, 56 patients were included, with an average age of 43±14.7 years and an average hospital stay of 22.25±11.6 days. Trauma types varied, with a significant proportion resulting from traffic accidents and burns. In 2022, 21 patients (average age 43.9±12.2 years) had longer hospital stays (37.5±23.4 days). The primary diagnoses included osteomyelitis and acute injuries. In 2023, 33 patients were studied, with a mean age of 42.5±27 years and an average stay of 12.6±11 days. Notably, the proportion of patients with osteomyelitis increased over the 3 years. Microbiological analysis revealed a growing presence of antibiotic-resistant pathogens.

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Abstract

Staphylococcus aureus (24%) and Pseudomonas aeruginosa (12%) were the most commonly isolated bacteria, with a significant increase in resistance to beta-lactams and other antibiotic groups. The emergence of multi-drug resistant *Klebsiella pneumoniae* and *Acinetobacter* species was also observed. The study highlights a concerning trend of increasing antibiotic resistance in pathogens isolated from infected wounds. This underscores the need for ongoing surveillance, updated treatment protocols, and the judicious use of antibiotics to manage such infections effectively. Further research is required to develop strategies to combat the rise of antibiotic-resistant infections.

Keywords: wound infections, microbiological profile, antibiotic resistance, injury mechanisms, surgical interventions, comorbidities

1. Introduction

Surgical closure of wound defects is a key procedure in treating patients with various injuries and chronic conditions leading to wound formation. These operations aim to restore skin integrity, prevent infection, and accelerate the healing process [1, 2]. However, a major challenge in modern medicine is the increasing number of infections caused by antibiotic-resistant microorganisms.

Antibiotic resistance is the ability of bacteria to withstand the effects of antibiotics, significantly complicating the treatment of infectious diseases and increasing the risk of complications and mortality [3–5]. In recent years, there has been a substantial increase in resistant strains, particularly among pathogens such as *Staphylococcus aureus* (including MRSA), *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumonia* [6]. These microorganisms often cause complex wound infections, necessitating thorough microbiological monitoring and adaptation of therapeutic strategies [7–8].

Timely and accurate identification of infection pathogens and their antibiotic sensitivities play a crucial role in selecting effective treatments and preventing the spread of resistant strains. Therefore, studying the dynamics of microbiological profiles and microorganism resistance over different periods becomes a relevant task for medical institutions [9–12].

The 2019 World Economic Forum report in Davos, Switzerland, highlights the urgent need for action against the "rapid and massive spread of infectious diseases," which is one of the greatest threats to human health (World Economic Forum, 2019). Infections caused by antibiotic-resistant bacteria are responsible for approximately 700,000 deaths annually worldwide and are estimated to cause more than 10 million deaths per year by 2050 [13].

This retrospective study aims to analyze the microbiological data of patients who underwent surgical wound defect closure in 2021, 2022, and 2023. Special attention is given to the dynamics of antibiotic-resistant strains, which allows for assessing the effectiveness of current treatment methods and identifying the need for developing new strategies for preventing and treating infections.

2. Materials and Methods

2.1. Study design

The present study is a retrospective analysis of data pertaining to patients who underwent surgical procedures for the closure of wound defects between 1 January 2021 and 31 December 2023. The study was conducted at the National Scientific Centre of Traumatology and Orthopaedics, named after Academician Batpenov N.D. The sampling by year was due to the number of hospitalizations in the specified time periods of patients meeting the inclusion criteria, so there was patient variability. Nevertheless, the general pattern of increasing antibiotic resistance is evident.

The following patients were included in the study:

- The study included case histories of patients treated at the National Scientific Centre of Traumatology and Orthopaedics Astana between 2021 and 2023.
- Availability of patient complete medical records, including data on microbiological analysis.
- In each case, bacteriological studies (culture) were performed to assess the microbial flora.
- The patients had wound defects requiring surgical closure through surgical interventions.

The following criteria resulted in exclusion from the study:

- Lack of availability of bacteriological culture or lack of data on the results of bacteriological examination.
- Presence of wound defects that could be eliminated without surgical intervention or on an outpatient basis.

The surgical procedure to close the wound defect was performed. The period of hospitalization spanned the years 2021 to 2023.

While retrospective studies provide valuable insights, they are inherently limited by the quality and completeness of the available records. In this study, we have taken measures to minimize potential biases by conducting a thorough review of patient records and excluding cases with significant missing data. For instances where data were incomplete but not critical to the analysis, we employed statistical methods such as multiple imputations to estimate missing values. This approach helps mitigate the impact of missing data on the overall findings, ensuring the robustness of our conclusions.

2.2. Data collection

The data for analysis were collected from the patients' electronic medical records. The data collected included the following parameters:

1. Demographic data: age

The study was conducted over a period of 3 years to analyze the results of surgical procedures aimed at closing wound defects in 110 patients. The mean age of the patients was 42.6 years, which reflects the considerable age range of the cases included in the study. The duration of postoperative hospitalization exhibited considerable variation according to the year and type of injury, with an average of 24.1 bed days.

2. Clinical characteristics:

The number of bed days in the ward was also recorded, as was the presence of comorbidities, including diabetes mellitus, arterial hypertension, chronic lung diseases, among others.

The length of hospitalization following surgery varied according to the year and type of injury, with an average of 24.1 bed days.

Injury characteristics included the type of injury (acute or chronic), as well as the localization of the wound defect (lower limbs, upper limbs, trunk).

2.3. Statistical analysis

Statistical analysis was performed using SPSS software version 25.0. Demographic and clinical data are presented as means and standard deviations for continuous variables, and as frequencies and percentages for categorical variables. Comparison of data by years was conducted using the Kruskal-Wallis test for continuous variables and the chi-square test for categorical variables. *P*-values <0.05 were considered statistically significant.

To more accurately analyze the factors influencing the rise in antibiotic resistance, a multivariate logistic regression was conducted. The dependent variable was the presence or absence of antibiotic resistance in isolated strains of *S. aureus* and *P. aeruginosa*. Independent variables included patient age, gender, length of hospital stay, presence of comorbidities (such as diabetes mellitus, ischemic heart disease), and the year of observation (2021, 2022, or 2023).

3. Results

Bacteriological analyses constituted a significant component of the study. The most frequently identified pathogens were *S. aureus* (24%), *P. aeruginosa* (12%) and *K. pneumoniae* (9%) (Tables A.1 and A.2). Of particular interest was the observed trend of increasing antibiotic resistance (Table A.3).

The analysis of bacterial resistance to antibiotics revealed a significant prevalence of resistance cases, particularly in *S. aureus* to beta-lactam antibiotics and in *P. aeruginosa* to cephalosporins. This highlights the necessity for uninterrupted observation of antibiotic resistance and the formulation of bespoke strategies for the treatment of postoperative infections (Figure **1**).

It is recommended that all outcomes be considered in greater detail by year. The 2021 study of wound defect closure by surgical techniques included 56 patients with a mean age of 43 years (standard deviation 14.7 years). The demographic and characteristic data for this cohort are presented in the following section.

The mean number of bed days was 22.25 (standard deviation 11.6). The patient cohort comprised 32 males (57.1%) and 24 females (42.9%).

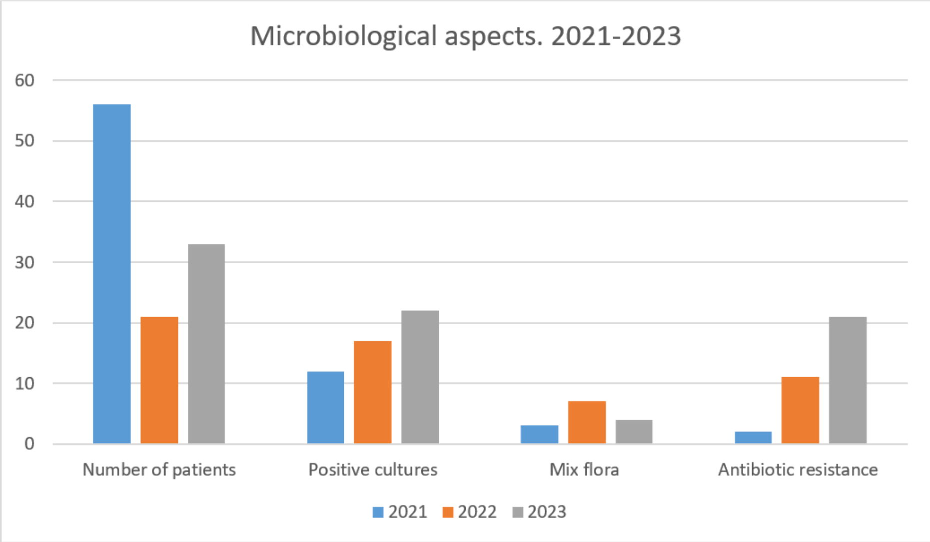

Figure 1: Comparative microbiological characteristics of wound infections from 2021 to 2023, including number of patients, positive cultures, mixed flora, and antibiotic resistance.

3.1. Injury types and their mechanisms

Injuries and their mechanisms were classified into two categories: acute conditions, which were recorded in 15 patients (26.8%), and chronic conditions, which were observed in 41 patients (73.2%). Injuries resulting from road traffic accidents were observed in 17 patients (30.4%), injuries due to temperature exposure were observed in 11 patients (19.6%), injuries due to high-altitude exposure were observed in three patients (5.4%), and injuries due to exposure to complex mechanisms at home and at work were observed in 11 patients (19.6%). Postoperative conditions were observed in seven patients (12.5%), one patient sustained an injury from a dog bite (1.8%), and one patient suffered from a congenital disease (1.8%).

The distribution of injuries by location and type is as follows: upper limb injuries were recorded in 16 cases (28.6%), lower limb injuries in 35 cases (62.5%), body injuries in 1 case (1.8%), and head injuries in 3 cases (5.4%).

3.2. Comorbidities

Comorbidities were identified among the patients, including arthritis in one patient (1.8%), coronary heart disease (CHD) in seven patients (12.5%), and diabetes mellitus in two patients (3.6%). Additionally, respiratory pathologies were observed in two patients (3.6%), cancer in two patients (3.6%), and hepatitis C in four patients (7.1%).

On admission, 17 patients (30.4%) had been diagnosed with sequelae of trauma and four patients (7.1%) had been diagnosed with burns. These constituted the total number of injuries (11 cases).

In 2021, the following surgical procedures were performed:

1. Two-stage surgeries:

a. In 23 cases, operations were conducted in two stages (41.1%), of which five required initial stage cardiopulmonary resuscitation (CPR) and 18 commenced with necrosectomy.

b. Operations utilizing free autodermoplasty with split skin flap:

i. Thirty-nine operations were performed (69.6%). This method provides a large surface area and comprehensive coverage, which facilitates successful healing.

c. Surgical procedures utilizing autodermoplasty with a vascular pedicle:

i. Eight surgical procedures were performed (14.3%). This technique enhances blood supply and the survival of the grafted flap.

d. Local tissue grafting of the wound defect:

i. Seven operations were performed (12.5%). This method mitigates the risk of rejection by utilizing the patient's endogenous tissue (Table A.4).

The following bacteriological results were obtained:

S. epidermidis was identified in four cases. *S. aureus* was identified in 13 cases, with one instance of resistance to cefazolin and one to azithromycin. *E. coli* was identified in three cases, one of which exhibited resistance to cefotaxime. *E. aerogenes* was identified in three cases. *P. aeruginosa* was identified in two cases, while *Citrobacter freundii* was identified in a single case. *A. baumannii* was identified in a single case.

In 2022, a total of 21 patients underwent surgical closure of wound defects. The average patient age was 43.9 years (±12.2), and the mean duration of hospitalization was 37.5 days (±23.4). The leading causes of injury were road traffic accidents (RTA), which accounted for eight cases (38.1%), followed by gunshot wounds in three cases (14.3%). Single cases (4.8% each) were reported for burns, falls from height, and trophic ulcers associated with underlying comorbidities. Regarding admission diagnoses, osteomyelitis was present in 13 patients (61.9%), acute trauma in six patients (28.6%), and post-traumatic complications in two patients (9.5%). Comorbid conditions were common: eight patients (38.1%) had acute pathological processes, while 13 patients (61.9%) presented with chronic diseases.

Injury localization was predominantly in the lower extremities (18 cases, 85.7%), while upper extremity involvement was observed in three cases (14.3%). Microbiological analysis of wound cultures revealed the presence of monoflora in 11 cases (52.4%), with Gram-negative rods identified in seven cases—comprising *P. aeruginosa* (four cases), *K. pneumoniae* (two cases), and *Klebsiella oxytoca* (1 case). Gram-positive cocci, namely *S. aureus*, were detected in four cases. Mixed microbial flora was observed in five patients (23.8%), including four cases with *S. aureus* combined with other microorganisms and one case involving *Proteus vulgaris* and *P. aeruginosa*. No bacterial growth was detected in the remaining five cases (23.8%).

Antibiotic resistance profiling revealed alarming trends. Among *P. aeruginosa* isolates, resistance was observed to amoxiclav and cefuroxime (one case), ciprofloxacin and levofloxacin (one case), and a broader multidrug resistance profile (one case) including amikacin, ciprofloxacin, gentamicin, meropenem, levofloxacin, and ticarcillin. Additionally, one isolate showed resistance to amoxicillin. *S. aureus* strains demonstrated resistance to imipenem (one case), azithromycin (three cases), and ampicillin (four cases). Extended-spectrum beta-lactamase (ESBL) producing *K. pneumoniae* showed resistance to amoxiclav and all beta-lactam antibiotics, indicating a significant therapeutic challenge in managing these infections.

Among the 16 cases with positive bacteriological cultures, Gram-positive cocci and Gram-negative rods were identified with nearly equal frequency. Gram-negative rods were detected in seven cases (43.8%), while Gram-positive cocci were present in eight cases (50.0%). Mixed flora was found in several specimens and included combinations of both Gram-positive and Gram-negative microorganisms, indicating the polymicrobial nature of certain wound infections.

The antibiotic susceptibility analysis revealed a significant level of resistance among the isolated pathogens. The most notable resistance was observed among Gram-negative rods, particularly *P. aeruginosa*, and Gram-positive cocci, predominantly *S. aureus*. Resistance to beta-lactam antibiotics was reported in *P. aeruginosa*, including resistance to amoxiclav, cefuroxime, and ticarcillin. ESBL-producing *K. pneumoniae* demonstrated resistance to all beta-lactam antibiotics tested. Furthermore, resistance to fluoroquinolones (ciprofloxacin and levofloxacin) and aminoglycosides (amikacin and gentamicin) was documented in *P. aeruginosa* isolates. Among the *S. aureus* strains, resistance was noted against macrolides (azithromycin), carbapenems (imipenem), and penicillins (ampicillin). These findings emphasize the growing challenge of antibiotic resistance in chronic wound management and underline the need for targeted antimicrobial stewardship strategies.

In 2023, a total of 33 patients underwent surgical procedures for wound defect closure. The average age of the patients was 42.5 years (±27), and the mean hospital stay duration was 12.6 days (±11). The primary mechanisms of injury included road traffic accidents in 12 cases (36.4%), falls from height in seven cases (21.2%), and injuries related to complex household and industrial mechanisms in five cases (15.2%). Isolated cases (3.0% each) were associated with dog bites, post-injection complications, gunshot wounds, burns, postoperative wound complications, compression from plaster casts, and direct trauma to the teeth.

Upon admission, most patients (23 cases, 69.7%) were diagnosed with osteomyelitis. Acute trauma and trauma sequelae were each observed in five patients (15.2%). Injury localization was predominantly in the lower extremities (25 patients, 75.8%), while upper extremity and head injuries were reported in seven (21.2%) and one (3.0%) patients, respectively.

Bacteriological examination revealed monomicrobial cultures in 18 cases (54.5%). Gram-positive cocci were the predominant isolates, including seven cases (21.2%) of *S. aureus*, with one methicillin-resistant strain (MRSA, 3.0%), and four cases (12.1%) of *Staphylococcus epidermidis*, also with one MRSA isolate.

Among Gram-negative organisms, *P. aeruginosa* was isolated in five cases (15.2%). Mixed microbial flora was identified in four cases (12.1%), and no bacterial growth was observed in 11 cases (33.3%).

Comorbid conditions were present in a subset of patients, with arterial hypertension reported in five individuals (15.2%), diabetes mellitus in two patients (6.1%), and one case each (3.0%) of oncologic disease, Charcot-Marie-Tooth syndrome, hepatitis C, and chronic respiratory pathology.

Surgical interventions for wound closure included free split-thickness skin grafting in 11 patients (33.3%), rotational flap surgeries in nine patients (27.3%), and local tissue closure techniques in 13 patients (39.4%). The choice of surgical method was individualized based on wound characteristics, location, and patient condition.

Additionally, a microbiological profile analysis was conducted. The microbial profile is characterized by the prevalence of molds. Gram-positive cocci represent the majority of the isolates (61.1%), indicating their role in the pathogenesis of infections following traumatic injuries. The issue of antibiotic resistance is a significant concern in the field of microbiology. It is imperative to give due consideration to the distribution of microbial resistance to antibiotics.

In 2023, *S. aureus* isolates demonstrated a high level of antibiotic resistance. Complete resistance was observed across several antibiotic classes, including beta-lactam antibiotics, meropenem, ciprofloxacin, levofloxacin, and ticarcillin. Additionally, two separate isolates exhibited resistance to azithromycin and third-generation cephalosporins such as cefotaxime. Others showed resistance to combinations such as amoxicillin with clavulanate and ampicillin with azithromycin. Methicillin-resistant *S. aureus* (MRSA) strains were identified, indicating resistance to beta-lactam antibiotics due to altered penicillin-binding proteins.

Among coagulase-negative staphylococci, one case of methicillin-resistant *S. epidermidis* (MRSE) was detected, also demonstrating resistance to methicillin. All *K. pneumoniae* isolates identified as ESBL-producing strains showed resistance to cefazolin series antibiotics (cefazolin, cefuroxime), as well as to levofloxacin, ticarcillin, and tetracycline. However, these isolates remained susceptible to carbapenems, including doripenem, meropenem, and imipenem.

A single isolate of *Acinetobacter baumannii* exhibited multidrug resistance, with susceptibility preserved only to doripenem, gentamicin, tetracycline, and meropenem. Importantly, across all examined pathogens, no resistance to the fourth-generation cephalosporin cefepime was detected, highlighting its continued effectiveness in the current antimicrobial landscape.

No statistically significant difference was observed in the age of the patients, including in age between the various years ($p = 0.9866$). (Figure **2**).

The number of bed days for patients in 2021 ($M = 22.250$) was found to be statistically significantly less than that for patients in 2022 ($M = 37.524$), p =0,000675277146 (Figure **3**).

According to the Kruskal-Wallis test, there is a statistically significant difference. However, a pairwise comparison using the Bonferroni test revealed that this difference is exclusive to the comparison between 2021 and 2022 (Tables **1** and **2**).

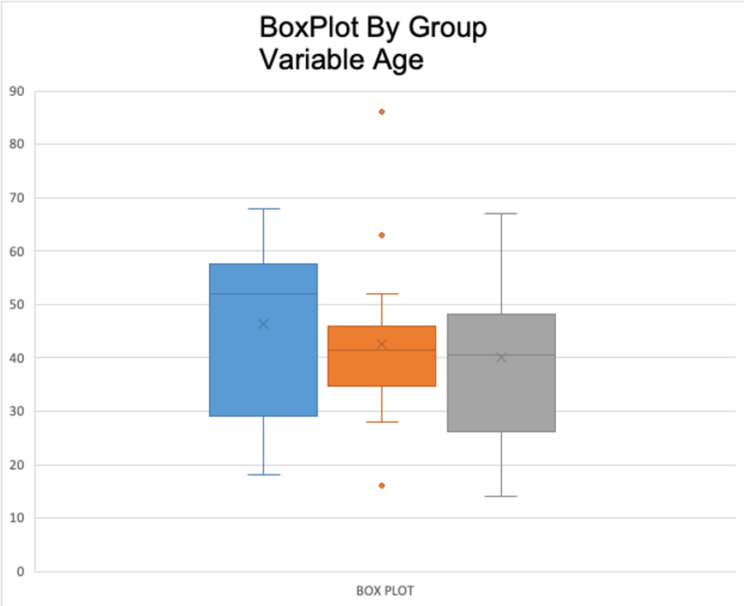

Figure 2: Distribution of patient age across study groups (2021–2023) based on boxplot analysis.

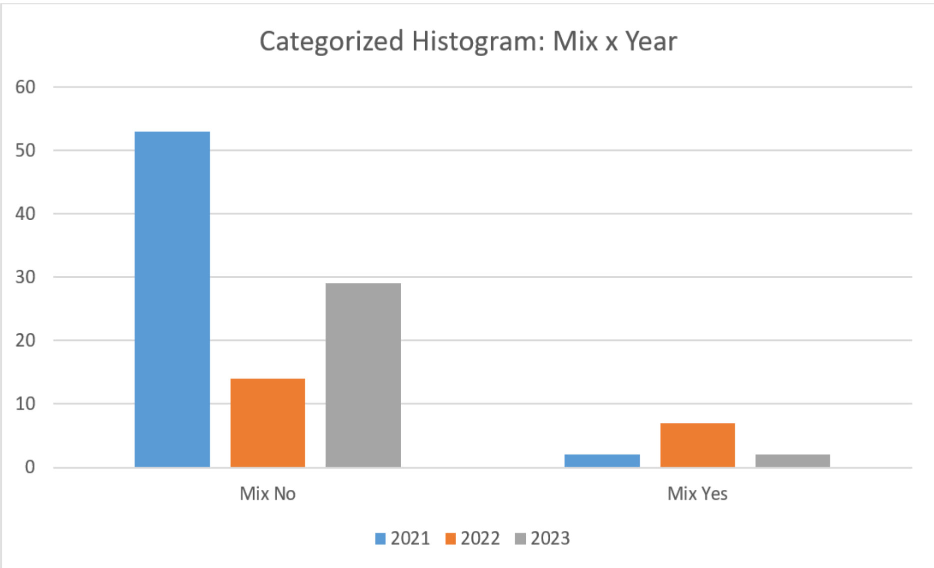

Figure 3: Frequency of mixed microbial flora in wound cultures by year (2021–2023).

Table 1: Comparison of hospital bed days across years (2021–2023) using Kruskal–Wallis ANOVA by ranks.

Depend: Bed days in Hospital	Kruskal-Wallis ANOVA by Ranks; Bed days in Hospital Grouping variable; Year Kruskal- Wallis test: H (2, N=110) = 7.5477774, p=.0230			
	Code	Valid N	Sum of Ranks	Mean Rank
2021	2021	56	2709.500	48.38393
2022	2022	21	1476.500	70.30952
2023	2023	33	1919.000	58.15152

In order to compare qualitative attributes, Pearson's Chi-square test was employed. A statistically significant difference was observed in the resistance of the flora between the years 2021 and 2023.

Table 2: Post hoc comparison of hospital bed days between years (2021–2023) using Bonferroni test.

Cell No.	Bonferroni Test; Variable Bed Days in Hospital (Probabilities for Post Hoc Tests Error: Between MS = 244,31, df = 107,00			
	Year	{1} 22,250	{2} 37,524	{3} 27,182
1	2021		0,000675	0,460232
2	2022	0,000675		0,058689
3	2023	0,460232	0,058689	

χ^2 = 37,5671 *p*-value = 0.000000 Degrees of freedom (dof) = 2. Since the *p*-value is less than 0.05, it can be concluded that there are significant differences in the distribution of resistance over the years (Table **3**).

Table 3: Distribution of antibiotic resistance by year (2021–2023) with Pearson Chi-square test of independence.

Summary Table: Expected Frequencies Spreadsheet Final General Marked Cells Have Counts >1. Pearson Chi-square: 37,5671, df=2, p=,000000				
Resistance	Year 2021	Year 2022	Year 2023	Row Totals
No	38,18182	14,31818	22,50000	75,0000
Yes	17,81818	6,68182	10,50000	35,0000
All groups	56,00000	21,00000	33,000000	110,0000

Results of the Pearson Chi-Square analysis for comparing bacteriological data (difference between monoflora and mixed flora) over 3 years:

χ^2 = 10.777 *p*-value = 0.0046 Degrees of freedom (dof) = 2

Expected values:

For 2021: monoflora - 48.87, mixed flora - 7.13 For 2022: monoflora - 18.33, mixed flora - 2.67 For 2023: monoflora - 28.8, mixed flora - 4.2

Since the *p*-value is less than 0.05, it can be concluded that there are significant differences in the distribution of monoflora and mixed flora over the years (Table **4**).

Table 4: Distribution of mixed microbial flora by year (2021–2023) with Pearson Chi-square test of independence.

Summary Table: Expected Frequencies Spreadsheet Final General Marked Cells Have Counts >1. Pearson Chi-square: 10,7773, df=2, p=,004568				
Mix	Year 2021	Year 2022	Year 2023	Row Totals
No	48,87273	18,32727	28,800000	96,0000
Yes	7,12727	2,67273	4,20000	14,0000
All groups	56,00000	21,00000	33,00000	110,0000

The results of the statistical analysis corroborate the observation of an annual increase in crop resistance and the prevalence of mixed flora.

Separate logistic regression models were constructed for each microorganism. For example, in the case of MRSA, the results indicated that an increase in age by 10 years was associated with a 15% rise in the likelihood of MRSA (odds ratio [OR] = 1.15, 95% confidence interval [CI]: 1.05-1.27, $p < 0.01$). The presence of diabetes mellitus increased the odds of resistance by 1.6 times (OR = 1.60, 95% CI: 1.10-2.34, $p < 0.05$). The year of observation also showed a significant effect: compared to 2021, the likelihood of encountering MRSA in 2023 increased by 1.9 times (OR = 1.90, 95% CI: 1.30-2.76, $p < 0.001$).

For carbapenem-resistant *P. aeruginosa*, significant results were also observed: the presence of ischemic heart disease increased the likelihood of resistance by 25% (OR = 1.25, 95% CI: 1.01-1.54, $p < 0.05$), while a hospital stay longer than 20 days increased it by 40% (OR = 1.40, 95% CI: 1.20-1.65, $p < 0.01$). The year of observation also had a significant impact on the likelihood of resistance ($p < 0.01$).

These results suggest statistically significant relationships between the selected factors and the rise in antibiotic resistance, indicating potential temporal trends and the influence of individual patient characteristics on the likelihood of developing resistance.

4. Discussion

A discussion of the global impact of antibiotic-resistant microorganisms reveals an estimated 10 million deaths per year by 2050, making it a leading cause of death with an economic loss of up to $100 trillion [14]. The global increase in antibiotic resistance is observed on an annual basis.

For example, a study conducted in Japan in 28 hospitals over a 2-year period also demonstrated an increase in microbial resistance to antibiotics [15]. Furthermore, the emergence of antibiotic resistance complicates the selection of appropriate antibiotics and necessitates the development of new ones. This imposes an economic burden on the healthcare system, as evidenced by the study conducted by Pink et al. [16].

For example, Pulingam et al. indicate that the mechanisms of bacterial resistance to antibiotics are categorized into three general pathways [17]. These include alteration of the antibiotic target site, modification or degradation of the antibiotic molecule, and finally, inhibition of antibiotic binding to the target site through an elimination method. Furthermore, resistance genes are typically acquired by bacteria through transformation (uptake of a resistant gene from the environment), transduction (transfer of a resistant gene from a bacteriophage), and bacterial conjugation (transfer of a resistant gene between resistant bacterial strains) [17]. The social component should also not be overlooked, with researchers from India highlighting the unjustified sale of antibiotics without prescription, inadequate sanitation, and the dumping of unmetabolized antibiotics or their residues with feces/dung and industrial effluents into the environment as a major factor in increasing antibiotic resistance [18].

Consequently, the predominant bacterial infections observed in bacteriological cultures were *S. aureus*, *P. aeruginosa*, and *K. pneumonia*, which demonstrate an annual increase in antibiotic-resistant forms worldwide [19, 20]. It is notable that the number of bed days remained stable despite an increase in resistant cultures and the prevalence of mixed forms. This is in contrast to studies conducted in Australia, which suggest that despite an increased frequency, the total number is not critical [21].

The increase in antibiotic resistance after systemic and prolonged use was confirmed in a study of changes in antibiotic sensitivity in the United States, which showed an expansion of antimicrobial resistance in *S. epidermidis*, one of the most common species in skin microbial communities and important nosocomial pathogens [22].

To effectively manage antibiotic resistance, several additional strategies can be implemented. Key measures include conducting educational programs for healthcare professionals and the public, implementing antibiotic stewardship programs in healthcare facilities, and developing new antibiotics and alternative treatments such as bacteriophages and probiotics [23]. It is also important to reduce the use of antibiotics in veterinary medicine and to develop international cooperation for sharing best practices and strategies to combat resistance. These approaches can significantly improve outcomes and complement existing surveillance methods and guideline updates [24].

The latest developments and strategies are being proposed to combat antibiotic resistance worldwide. For example, combinations of antibacterial agents show significantly better results in eradication of bacterial agents and cure of patients compared to the use of a single antibiotic in monotherapy [25]. Certainly, one strategy involves the development of new antimicrobials that affect not only the structure of the cell but also its genome, as was presented at a recent WHO congress [26].

Nevertheless, it should be noted that the present study is not without limitations. For instance, the study was conducted in a single healthcare facility, which may restrict the capacity to generalize the findings to other conditions. It would be beneficial for future studies to consider a longer time frame, a larger cohort of patients, and multiple inpatients.

5. Conclusion

The study offers a comprehensive overview of the evolution of the microbiological and antibiotic resistance landscape in wound infections over a 3-year period. Notwithstanding its limitations, the study underscores the imperative for targeted antibiotic use policies and enhanced clinical protocols to address the mounting challenge of antibiotic resistance. It would be beneficial for future studies to include larger, multi-center cohorts in order to enhance the general applicability and reliability of the findings.

The study corroborates the necessity for systematic monitoring and adaptation of treatment strategies. The results highlight the global need to revise approaches to antibiotic use and improve clinical protocols to address the growing threat of resistance. The effective measures and strategies identified in this research can serve as a foundation for developing international standards and recommendations, promoting more targeted antibiotic management and preventing global epidemics.

Author Contribution

A.A.M. - Conducted the study and data analysis. S.D.A. – Responsible for data collection and writing the “Materials and Methods” section. R.D.V.- Responsible for data processing and writing the “Results” section. Batpen A.N. – Responsible for the statistical analysis and writing the “Discussion” section. B.S.S. - Responsible for the study design development work coordination. R. Zh.K. – Wrote the literature review and the introduction. A.G.O. Interpreted the results and wrote the conclusion. K.A.A. - Responsible for data verification and editing the article. M.A.V. - Responsible for data collection and contributed to writing the “Materials and Methods” section. A.Zh.S. – Responsible for data visualization and preparation of figures and diagrams. K.G.K. -Responsible for reviewing related studies and contributed to writing the “Discussion” section.

Appendix

Table A.1: Distribution of monomicrobial isolates from wound cultures in 2021–2023.

Microorganisms (monoflora)	2021	2022	2023
S. aureus	13 (23.2%)	4 (19%)	7 (21.2%)
S. epidermidis	4 (7.1%)	-	4 (12.1%)
E. coli	3 (5.3%)	-	-
E. aerogenes	3 (5.3%)	-	-
P. aeruginosa	2 (3.6%)	4 (19%)	5 (15.2%)
Citrobacter	1 (2%)	-	-
A. baumannii	1 (2%)	-	-

Table A.2: Composition of mixed microbial flora isolated from wound cultures in 2021–2023.

Mixed flora (multiple microorganisms)	2021	2022	2023
	-	5 (23.8%)	4 (12.1%)
S. aureus + *K. oxytoca*	-	2 (9.5%)	-
S. aureus + *P. vulgaris*	-	2 (9.5%)	-
S. aureus + *C. diversus*	-	3 (14.3%)	-
P. vulgaris + *P. aeruginosa*	-	1 (4.8%)	-
S. aureus + *P. aeruginosa*	-	-	2 (6.1%)
K. pneumoniae ESBL + *S. aureus* MRSA	-	-	1 (3%)

Table A.3: Identified antibiotic resistance patterns among isolated pathogens in 2021–2023.

Antibiotic Resistance	2021	2022	2023
S. aureus	1 (1.8%) to cefazolin	1 (4.8%) to ampicillin	1 (3%) to ampicillin
	1 (1.8%) to azithromycin	3 (14.3%) to azithromycin	1 (3%) to azithromycin
	-	-	1 (3%) to amoxicillin
P. aeruginosa	1 (1.8%) to cefotaxime	1 (4.8%) to cefotaxime	1 (3%) to cefotaxime
	-	1 (4.8%) to ceftazidime	1 (3%) to ceftazidime
	-	1 (4.8%) to cefuroxime	1 (3%) to cefuroxime
	-	1 (4.8%) to meropenem	1 (3%) to meropenem
	-	1 (4.8%) to ciprofloxacin	1 (3%) to ciprofloxacin
	-	1 (4.8%) to levofloxacin	1 (3%) to levofloxacin
K. pneumoniae ESBL	-	2 (9.5%) to amoxiclav	-
	-	2 (9.5%) to cefazolin	-
A. baumannii	-	-	1 (3%) to ticarcillin

Table A.4: Comparative characteristics of patients who underwent surgical closure of wound defects in 2021–2023.

Parameters	2021	2022	2023
Number of patients	56	21	33
Average age (years)	43 ± 14.7	43.9 ± 12.2	42.5 ± 27
Number of bed days	22.25 ± 11.6	37.5 ± 23.4	12.6 ± 11
Types of injuries and mechanisms of occurrence			
Road traffic accidents (RTA)	17 (30%)	8 (38.1%)	12 (36.4%)
Thermal injuries	11 (20%)	1 (4.8%)	1 (3.0%)
Falls from height	3 (5%)	1 (4.8%)	7 (21.2%)
Injuries from household and industrial machinery	11 (20%)	-	5 (15.2%)
Post-operative injuries	7 (12.5%)	-	1 (3.0%)
Dog bites	1 (2%)	-	1 (3.0%)
Trophic ulcers due to accompanying diseases	-	1 (4.8%)	-
Gunshot wounds	-	3 (14.3%)	1 (3.0%)
Burns	-	1 (4.8%)	1 (3.0%)
Post-injection injuries	-	-	1 (3.0%)
Casting injuries	-	-	1 (3.0%)
Tooth impact injuries	-	-	1 (3.0%)
Injuries by localization			
Upper extremities	16 (28.6%)	3 (14.3%)	7 (21.2%)
Lower extremities	35 (62.5%)	18 (85.7%)	25 (75.8%)
Body	1 (1.8%)	-	-
Head	3 (5.4%)	-	1 (3.0%)
Diagnoses			
Sequelae of injuries	17 (30%)	2 (9.5%)	5 (15.2%)
Osteomyelitis	-	13 (61.9%)	23 (69.7%)
Acute traumas	11 (19.6%)	6 (28.6%)	5 (15.2%)
Bacteriological cultures			
Conducted	49 (87.5%)	16 (76.2%)	22 (66.7%)
Not conducted	7 (12.5%)	5 (23.8%)	11 (33.3%)
Microorganisms (monoflora)			
S. aureus	13 (23.2%)	4 (19.0%)	7 (21.2%)
S. epidermidis	4 (7.1%)	-	4 (12.1%)
P. aeruginosa	2 (3.6%)	4 (19.0%)	5 (15.2%)
E. coli	3 (5.4%)	-	-
E. aerogenes	3 (5.4%)	-	-
Citrobacter	1 (1.8%)	-	-
A. baumannii	1 (1.8%)	1 (4.8%)	-
K. pneumoniae ESBL	-	2 (9.5%)	-
Microorganisms (microflora)			
Mixed flora	-	5 (23.8%)	4 (12.1%)
Antibiotic resistance			
S. aureus	2 (15.4%)	4 (36.4%)	7 (33.3%)
P. aeruginosa	2 (15.4%)	5 (45.5%)	4 (18.2%)
K. pneumoniae ESBL	1 (7.7%)	1 (9.1%)	1 (4.5%)
A. baumannii	1 (7.7%)	1 (9.1%)	1 (4.5%)
Comorbidities			
Arterial hypertension	1 (1.8%)	3 (14.3%)	5 (15.2%)
Diabetes mellitus (DM)	2 (3.6%)	2 (9.5%)	2 (6.1%)
Coronary artery disease (CAD) + DM	2 (3.6%)	-	1 (3.0%)

Table A.4: Continued.

CAD	7 (12.5%)	-	-
Respiratory diseases	2 (3.6%)	-	1 (3.0%)
Oncological diseases	2 (3.6%)	-	1 (3.0%)
Hepatitis C	4 (7.1%)	-	1 (3.0%)
Rheumatoid arthritis	-	1 (4.8%)	-
Charcot-Marie-Tooth syndrome	-	-	1 (3.0%)
Types of surgeries			
Autodermoplasty	39 (69.6%)	12 (57.1%)	11 (33.3%)
Local tissue plastic surgery	7 (12.5%)	7 (33.3%)	11 (33.3%)
Rotational flaps	-	2 (9.5%)	9 (27.3%)
Two-stage operations	23 (41.1%)	15 (71.4%)	7 (21.2%)
Necrosectomy	15 (26.8%)	8 (38.1%)	8 (24.2%)
Vacuum-assisted closure (VAC)	5 (8.9%)	7 (33.3%)	7 (21.2%)
Histological biopsy	2 (3.6%)	-	-

References

[1] Desvigne MN, Bauer K, Holifield K, Day K, Gilmore D, Wardman AL. Case report: Surgical closure of chronic soft tissue defects using extracellular matrix graft augmented tissue flaps. Front Surg. 2021;7:559450.

[2] Truskett PG. Antimicrobial resistance and antibiotic usage: What can surgeons do? ANZ J Surg. 2020;90(3):198–199.

[3] Abdelrazik E, El-Hadidi M. Tracking antibiotic resistance from the environment to human health. Methods Mol Biol. 2023;2649:289–301.

[4] Berndtson AE. Increasing globalization and the movement of antimicrobial resistance between countries. Surg Infect (Larchmt). 2020;21(7):579–585.

[5] Lightdale CJ. Endoscopes and antibiotic-resistant bacteria: Controlling the risk. Gastrointest Endosc Clin N Am. 2020;30(4):xiii–xiv.

[6] Wang G, Zhao G, Chao X, Xie L, Wang H. The characteristic of virulence, biofilm and antibiotic resistance of *Klebsiella pneumoniae*. Int J Environ Res Public Health. 2020;17(17):6278.

[7] Baquero F. Threats of antibiotic resistance: An obliged reappraisal. Int Microbiol. 2021;24(4):499–506.

[8] Martin JK 2nd, Sheehan JP, Bratton BP, Moore GM, Mateus A, Li SH, et al. A dual-mechanism antibiotic kills Gram-negative bacteria and avoids drug resistance. Cell. 2020;181(7):1518–1532.e14.

[9] Lugagne JB, Dunlop MJ. Anticipating antibiotic resistance. Science. 2022;375(6583):818–819.

[10] Morrison L, Zembower TR. Antimicrobial resistance. Gastrointest Endosc Clin N Am. 2020;30(4):619–635.

[11] Tang KW, Millar BC, Moore JE. Antimicrobial resistance (AMR). Br J Biomed Sci. 2023;80:11387.

[12] Shakerimoghaddam A, Moghaddam AD, Barghchi B, Sanani MG, Azami P, Kalmishi A, et al. Prevalence of Pseudomonas aeruginosa and its antibiotic resistance in patients who have received hematopoietic stem-cell transplantation; A globally systematic review. Microb Pathog. 2023;184:106368.

[13] Aslam B, Wang W, Arshad MI, Khurshid M, Muzammil S, Rasool MH, et al. Antibiotic resistance: A rundown of a global crisis. Infect Drug Resist. 2018;11:1645–1658.

[14] Wang H, Wang H, Yu X, Zhou H, Li B, Chen G, et al. Impact of antimicrobial stewardship managed by clinical pharmacists on antibiotic use and drug resistance in a Chinese hospital, 2010-2016: A retrospective observational study. BMJ Open. 2019;9(8):e026072.

[15] Oka K, Matsumoto A, Tetsuka N, Morioka H, Iguchi M, Ishiguro N, et al. Clinical characteristics and treatment outcomes of carbapenem-resistant Enterobacterales infections in Japan. J Glob Antimicrob Resist. 2022;29:247–252.

[16] Song P, Li W, Zhou Q. An outpatient antibacterial stewardship intervention during the journey to JCI accreditation. BMC Pharmacol Toxicol. 2014;15:8.

[17] Pulingam T, Parumasivam T, Gazzali AM, Sulaiman AM, Chee JY, Lakshmanan M, et al. Antimicrobial resistance: Prevalence, economic burden, mechanisms of resistance and strategies to overcome. Eur J Pharm Sci. 2022;170:106103.

[18] Samreen, Ahmad I, Malak HA, Abulreesh HH. Environmental antimicrobial resistance and its drivers: A potential threat to public health. J Glob Antimicrob Resist. 2021;27:101–111.

[19] Wang M, Wei H, Zhao Y, Shang L, Di L, Lyu C, et al. Analysis of multidrug-resistant bacteria in 3223 patients with hospital-acquired infections (HAI) from a tertiary general hospital in China. Bosn J Basic Med Sci. 2019;19(1):86–93.

[20] Tatullo M, Gandolfi MG. Cells: Are they (still) essential for dental regeneration? Cells. 2021;10(3):498.

[21] Rodriguez-Acevedo AJ, Lee XJ, Elliott TM, Gordon LG. Hospitalization costs for patients colonized with carbapenemase-producing Enterobacterales during an Australian outbreak. J Hosp Infect. 2020;105(2):146–153.

[22] Jo JH, Harkins CP, Schwardt NH, Portillo JA, Zimmerman MD, Carter CL, et al. Alterations of human skin microbiome and expansion of antimicrobial resistance after systemic antibiotics. Sci Transl Med. 2021;13(625):eabd8077.

[23] Rather MA, Gupta K, Mandal M. Microbial biofilm: Formation, architecture, antibiotic resistance, and control strategies. Braz J Microbiol. 2021;52(4):1701–1718.

[24] Uddin TM, Chakraborty AJ, Khusro A, Zidan BR, Mitra S, Emran TB, et al. Antibiotic resistance in microbes: History, mechanisms, therapeutic strategies and future prospects. J Infect Public Health. 2021;14(12):1750–1766.

[25] Shields RK, Nguyen MH, Chen L, Press EG, Potoski BA, Marini RV, et al. Ceftazidime-Avibactam is superior to other treatment regimens against carbapenem-resistant Klebsiella pneumoniae Bacteremia. Antimicrob Agents Chemother. 2017;61(8):e00883–17.

[26] Antibacterial agents in clinical development: An analysis of the antibacterial clinical development pipeline [Internet]. Geneva, Switzerland: World Health Organization; 2019. Available from: https://www.who.int/publications/i/item/9789240000193